Complete Summary

GUIDELINE TITLE

Antiviral therapy and prophylaxis for influenza in children.

BIBLIOGRAPHIC SOURCE(S)

American Academy of Pediatrics Committee on Infectious Diseases. Antiviral therapy and prophylaxis for influenza in children. Pediatrics 2007 Apr;119(4):852-60. [61 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

All clinical reports and policy statements from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed, revised, or retired at or before that time.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released:

- April 02, 2008, Relenza (zanamivir): GlaxoSmithKline informed healthcare professionals of changes to the warnings and precautions sections of prescribing information for Relenza. There have been reports (mostly from Japan) of delirium and abnormal behavior leading to injury in patients with influenza who are receiving neuraminidase inhibitors, including Relenza.
- March 4, 2008, Tamiflu (oseltamivir phosphate): Roche and the U.S. Food and Drug Administration (FDA) informed healthcare professionals of neuropsychiatric events associated with the use of Tamiflu, in patients with influenza. Roche has updated the PRECAUTIONS section of the package insert to include the new information and guidance under the Neuropsychiatric Events heading.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Influenza

GUIDELINE CATEGORY

Prevention
Treatment

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Pediatrics
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To offer guidance regarding antiviral treatment and prophylaxis to clinicians caring for children during yearly influenza epidemics and to provide resources for information on antiviral treatment in the event of an influenza pandemic

TARGET POPULATION

- Children with moderate to-severe influenza infection who may benefit from a decrease in the duration of symptoms
- High-risk children who have not yet received immunization and during the 2 weeks after immunization
- Unimmunized family members and health care professionals with close contact with high-risk unimmunized children or infants who are younger than 6 months
- Unimmunized staff and children in an institutional setting

INTERVENTIONS AND PRACTICES CONSIDERED

Antiviral therapy and prophylaxis for influenza with oseltamivir, zanamivir, amantadine, or rimantadine

MAJOR OUTCOMES CONSIDERED

Treatment

- Duration of influenza-attributable symptoms
- Incidence of acute otitis media
- Level of viral shedding

Prevention

- Protective efficacy
- Number of symptomatic cases of influenza

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not applicable

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Dosing Recommendations for Antiviral Agents for Treatment and Prophylaxis of Influenza

Drug	Formulations	Dosing Recommendations											
		Treatment					Prophylaxis						
		Children				Adults	Children				Adu		
Oseltamivir (Tamiflu)	75-mg capsule; 60 mg/5 mL suspension	For treatment, children ≥12 mo should receive approximately 4 mg/kg per d divided into 2 doses for a 5-d treatment course				150 mg/d divided into 2 doses for 5 days	≤15 kg 30 mg once daily	>15-23 kg 45 mg once daily	>23-40 kg 60 mg once daily	>40 kg 75 mg once daily	75 m once daily		
		≤15 kg 60 mg/d divided into 2 doses	>15-23 kg 90 mg/d divided into 2 doses	>23-40 kg 120 mg/d divided into 2 doses	>40 kg 150 mg/d divided into 2 doses								
Zanamivir (Relenza)	5 mg per inhalation (Diskhaler)	Children ≥7 y and Adults					Children ≥5 y and Adult						
		2 inhalations (10 mg total per dose), twice daily for 5 d					2 inhalations (10 mg total p dose), once daily for 10 d						
Amantadine (Symmetrel)	100-mg tablet; 50 mg/5 mL suspension	1-9 y		9-12 y		Adults	1-9 y		9-12 y		Adult		
		5-8 mg/kg per d as a single daily dose or divided		200 mg/d divided into 2 doses (not		200 mg/d, either as a single daily	Same as treatment dose[a,b]		Same as treatment dose[a,b]		Same a treatm dose[a,b]		

Drug	Formulations	Dosing Recommendations					
		Treatment			Prophylaxis		
		Children		Adults	Children		Adu
		into 2 doses but not to exceed 150 mg/d[a,b;] treat for 24-48 h after the disappearance of signs and symptoms	studied as a single daily dose)[a,b]; treat for 24-48 h after the disappearance of signs and symptoms	dose or divided into 2 doses[a,b]; treat for 24-48 h after the disappearance of signs and symptoms			
Rimantadine (Flumadine)	100-mg tablet; 50 mg/5 mL suspension	**1-9 y**	**≥10 y**	**Adults**	**1-9 y**	**≥10 y**	**Adult**
		Not FDA approved for treatment in children, but published data exist on safety and efficacy		200 mg/d, either as a single dose or divided into 2 doses[a]	5 mg/kg per d once daily not to exceed 150 mg[a,b]	200 mg/d, either as a single daily dose or divided into 2 doses[a,b]	200 mg/d, either a a single daily dose or divided into 2 doses[a,]
		6.6 mg/kg per d (maximum 150 mg/kg per d) divided into 2 doses	200 mg/d, either as a single daily dose or divided into 2 doses[a]				

[a] Amantadine and rimantadine should only be used for prophylaxis in winter seasons during which a majority of influenza A virus strains isolated are adamantine-susceptible; the adamantanes should not be used for primary therapy because of the rapid emergence of resistance. However, for those requiring adamantine therapy, a treatment course of approximately 7 days is suggested, or 24 to 48 hours after the disappearance of signs and symptoms.

[b] For prophylaxis, antiviral drugs should be continued for the duration of known influenza A in the community because of the potential for repeated and unknown exposures or until immunity can be achieved after immunization.

Indications for Therapy and Prophylaxis

Therapy

- Influenza infection of any severity in high-risk children (see definition of "high-risk" below) regardless of immunization status
- Any otherwise healthy child with moderate-to-severe influenza infection who may benefit from the decrease in duration of clinical symptoms documented to occur with therapy

Prophylaxis

- High-risk children during the 2 weeks after influenza immunization, if influenza is active in the community
- High-risk children for whom influenza vaccine is contraindicated
- Family members or health care providers who are unimmunized and are likely to have ongoing, close exposure to (1) high-risk, unimmunized children or (2) infants who are younger than 6 months

- Control of influenza outbreaks for unimmunized staff and children in a closed institutional setting with high-risk pediatric residents (e.g., extended-care facilities)
- As a supplement to immunization among high-risk children
- Postexposure prophylaxis in a family setting
- High-risk children and their family members and close contacts, as well as health care workers, when circulating strains of influenza virus in the community are not matched with vaccine strains

Infants And Children at High Risk of Complications From Influenza Include Those with:

- Ages between 6 and 24 months (no antiviral agent is currently approved for infants younger than 12 months)
- Asthma or other chronic pulmonary diseases such as cystic fibrosis
- Hemodynamically significant cardiac disease
- Immunosuppressive disorders or therapy
- Human immunodeficiency virus (HIV) infection
- Sickle cell anemia and other hemoglobinopathies
- Diseases requiring long-term aspirin therapy, such as rheumatoid arthritis or Kawasaki disease
- Chronic renal dysfunction
- Chronic metabolic disease such as diabetes mellitus
- Neuromuscular disorders, seizure disorders, or cognitive dysfunction that may compromise the handling of respiratory secretions

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of antiviral therapy and prophylaxis for influenza in children

POTENTIAL HARMS

- Anti-viral resistance, especially with amantadine and rimantadine
- The most common adverse drug effects noted were gastrointestinal tract disturbances, with vomiting in 14% of oseltamivir-treated children, compared with 8% of children who were given placebo.
- Unpublished safety data on oseltamivir were recently reviewed by the U.S. Food and Drug Administration (FDA) on the basis of reports of

neuropsychiatric events associated with patients treated for influenza with oseltamivir. Accurate data on the incidence of these events are not available, but they seem to be in the range of 1 in 10,000 to 100,000 treatment courses. On the basis of the FDA review, it is not known whether the spontaneous reports of neuropsychiatric behavior reflect a true adverse event caused by oseltamivir, perhaps with a greater incidence in populations with a certain genetic background; a result of central nervous system (CNS) infection caused by influenza virus; or a combination of both drug and virus in the CNS. There are no reports of neuropsychiatric events in adults or children receiving oseltamivir prophylaxis for influenza infection.

- Reported adverse effects in otherwise healthy children and adults were similar between those treated with zanamivir and those given placebo. However, concerns by the FDA regarding bronchospasm and decreased pulmonary function after inhalation of zanamivir in patients with underlying reactive airways disease, including asthma and chronic obstructive pulmonary disease, prompted warnings about the use of zanamivir in this population. Potential risks and benefits should be carefully weighed before treatment of these children. Monitoring of respiratory function should be considered if treatment is given.
- The most commonly occurring (5 to 10%) adverse events of amantadine treatment are nausea, lightheadedness, and insomnia. Those that occur infrequently (1 to 5%) include anxiety, nervousness, irritability, dry mouth, headache, fatigue, and diarrhea. The incidence of CNS adverse effects is twofold higher in those taking amantadine than in those taking rimantadine. Gastrointestinal adverse effects are equivalent between the 2 agents. These effects are dosage related and are usually mild, resolving when the agent is discontinued. Serious adverse effects have been reported in adults and are often associated with either high plasma drug concentrations in patients with renal insufficiency or in those with an underlying psychiatric or seizure disorder.
- No differences in adverse-event rates were noted between children treated with rimantadine and those treated with acetaminophen. In controlled studies in adults, no drug-attributable adverse effects occurred in more than 5% of the study subjects with the most commonly reported events being insomnia and dizziness.

QUALIFYING STATEMENTS

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- The guidance in this report does not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.
- No prospective human data currently exist on which to base recommendations for treatment of infections caused by potential H5N1 pandemic influenza virus strains.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Apr

GUIDELINE DEVELOPER(S)

American Academy of Pediatrics - Medical Specialty Society

SOURCE(S) OF FUNDING

American Academy of Pediatrics

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Committee on Infectious Diseases

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

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GUIDELINE AVAILABILITY

Electronic copies: Available from the American Academy of Pediatrics (AAP) Policy Web site.

Print copies: Available from American Academy of Pediatrics, 141 Northwest Point Blvd., P.O. Box 927, Elk Grove Village, IL 60009-0927.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on May 15, 2007. The information was verified by the guideline developer on May 23, 2007. This summary was updated by ECRI Institute on March 10, 2008 following the U.S. Food and Drug Administration (FDA) advisory on Tamiflu (oseltamivir phosphate). This summary was updated by ECRI Institute on April 9, 2008 following the U.S. Food and Drug Administration (FDA) advisory on Relenza (zanamivir).

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